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Serum Calprotection and metabolic markers in Osteoarthritis Patients

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ABSTRACT

Introduction: Osteoarthritis (OA) is a common degenerative joint disease characterized by pain, stiffness, and reduced mobility, mainly affecting the knees, hips, and hands. Recent evidence suggests that OA is not only a degenerative disorder but also involves inflammatory and metabolic mechanisms. Biomarkers such as calprotectin may help in assessing disease activity and severity in OA.
Objectives: To evaluate inflammatory markers including serum calprotectin, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), along with metabolic markers such as serum glucose, lipid profile, adiponectin, leptin, and resistin in OA patients, and to assess their association with disease severity and functional status.
Methods: This cross-sectional study was conducted over 12 months in the Departments of Biochemistry and Orthopedics and included 50 OA patients and 50 healthy controls. Blood samples were analyzed for glucose, lipid profile, adiponectin, leptin, resistin, and calprotectin using automated methods and ELISA. Pain severity, functional status, and disease staging were assessed using VAS score, KOOS questionnaire, and Kellgren–Lawrence grading system.
Results: OA patients had significantly higher body mass index and elevated levels of leptin, adiponectin, resistin, calprotectin, fasting blood sugar, LDL cholesterol, and ESR compared to controls. CRP and HDL cholesterol showed no significant difference. Most OA patients had Grade 2 or Grade 3 disease. KOOS scores were significantly lower in OA patients, indicating impaired knee function and reduced quality of life. Higher resistin and LDL cholesterol levels were associated with poorer KOOS scores, while calprotectin levels correlated significantly with OA grading.
Conclusion: The study demonstrates the important role of inflammatory and metabolic markers in OA. Elevated calprotectin and resistin levels may reflect disease severity and functional impairment, suggesting their potential use as biomarkers for assessing disease activity in osteoarthritis.

Keywords*: Osteoarthritis, Calprotectin, Inflammation, Metabolic Biomarkers, KOOS Questionnaire.*

INTRODUCTION

Osteoarthritis (OA) is a significant public health issue worldwide, primarily affecting the knees, hips, and hands. It leads to pain, stiffness, swelling, and decreased joint function. While OA was traditionally viewed as a non-inflammatory "wear and tear" condition, it is now understood to be a multifactorial disease characterized by chronic low-grade inflammation, immune responses, and cartilage degeneration. Key risk factors include aging, obesity, past joint injuries, repetitive stress, skeletal malalignment, and genetic factors. Current management strategies emphasize lifestyle changes, exercise, weight loss, and symptom relief through nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular treatments, as no disease-modifying therapies are available at this time.[1-4]

The progression of OA varies among individuals, and reliable biomarkers for evaluating disease activity and progression remain scarce. Traditional radiography only reveals late-stage structural changes, while magnetic resonance imaging (MRI) provides improved visualization of cartilage, synovium, menisci, ligaments, and subchondral bone. However, the high costs and lack of standardization of MRI limit its routine application. Thus, there is a growing demand for sensitive biochemical biomarkers to aid in the early diagnosis, monitor inflammation, and predict disease progression in OA[5-7].

Calprotectin (CLP), a heterodimer of S100A8 and S100A9 proteins, has emerged as a promising inflammatory biomarker for OA and other rheumatic diseases. It is primarily released by granulocytes and monocytes and plays a crucial role in inflammatory responses by enhancing cytokine production and cellular activation. Increased levels of S100A8/S100A9 in synovial macrophages have been linked to cartilage damage and synovial inflammation in OA. Serum calprotectin is already recognized as a valuable biomarker in conditions such as rheumatoid arthritis, psoriatic arthritis, and juvenile idiopathic arthritis. Therefore, measuring serum calprotectin levels in OA patients and comparing them to healthy controls may clarify its role as an inflammatory marker and disease activity indicator, alongside traditional markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [8-10].

Objectives:
The study aims to evaluate inflammatory markers such as serum calprotectin, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), along with metabolic markers including serum glucose, lipid profile, adiponectin, and resistin in osteoarthritis (OA) patients. It also seeks to compare serum calprotectin levels between OA patients and healthy controls and assess the association of these inflammatory and metabolic markers with pain severity and disease staging in OA patients.

METHODOLOGY:
This cross-sectional study was conducted over 12 months in the Departments of Biochemistry and Orthopedics at Srinivasan medical college and hospital, Samayapuram, Trichy. It included 100 participants, consisting of 50 patients with osteoarthritis (OA) and 50 healthy controls. Patients diagnosed with OA who attended the Orthopedics Department were enrolled after providing informed consent. Exclusions from the study included individuals on steroids or immunosuppressive medications, those with post-surgical cases, traumatic injuries, septic infections, malignancies, and pregnant women. Venous blood samples were collected under aseptic conditions to assess various biochemical parameters. Plasma glucose and lipid profiles were analyzed using a fully automated analyzer, while serum levels of adiponectin, leptin, resistin, and calprotectin were measured using commercial enzyme-linked immunosorbent assay (ELISA) kits. Demographic and anthropometric data were collected for all participants. Pain severity was evaluated using the Visual Analog Scale (VAS), functional status was assessed with the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire, and radiographic staging of OA was determined by an orthopedist according to the Kellgren–Lawrence grading system.

RESULTS:
A total of 100 participants were included in the study, comprising 50 osteoarthritis cases and 50 healthy controls. The mean age of cases and controls was 55.82 ± 10.43 years and 57.18 ± 10.48 years respectively, with no significant difference between the groups (p=0.517). Females constituted the majority of the study population, accounting for 57% of participants, while males accounted for 43%, and the sex distribution between cases and controls was statistically insignificant (p=0.703). The mean BMI was significantly higher among OA patients (26.19 ± 3.35 kg/m²) compared to controls (24.12 ± 2.76 kg/m²) (p=0.001), whereas no significant differences were observed in weight and height between the groups.

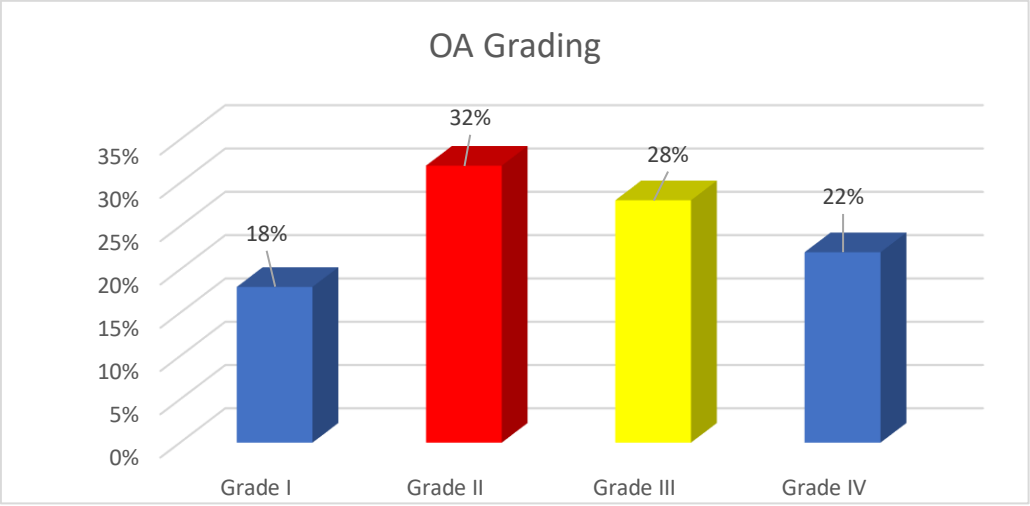

Figure1: OA Grading of Study Participants:

Biochemical investigations showed significantly higher levels of leptin, adiponectin, resistin, and calprotectin in osteoarthritis (OA) patients compared to healthy controls. Among these markers, serum calprotectin and resistin demonstrated highly significant elevation in OA patients ($p<0.001$). Fasting blood sugar (FBS), LDL cholesterol, ESR (1st and 2nd hour), and ESR (1st hour) were also significantly increased in cases compared to controls. However, CRP and HDL levels did not show statistically significant differences between the two groups. The mean KOOS score was significantly lower in osteoarthritis patients (70.80 ± 26.07) compared to healthy controls (94.62 ± 4.66), indicating poorer knee function and quality of life among OA patients ($p<0.001$). Correlation analysis showed that KOOS score had weak negative correlations with leptin, adiponectin, fasting blood sugar, and CRP levels. Moderate negative correlations were observed between KOOS score and resistin ($r=-0.323$, $p=0.001$) as well as LDL cholesterol ($r=-0.42$, $p<0.001$), indicating poorer knee function with increasing levels of these markers. HDL showed a weak positive correlation, while calprotectin demonstrated a weak positive but statistically insignificant correlation with KOOS score.

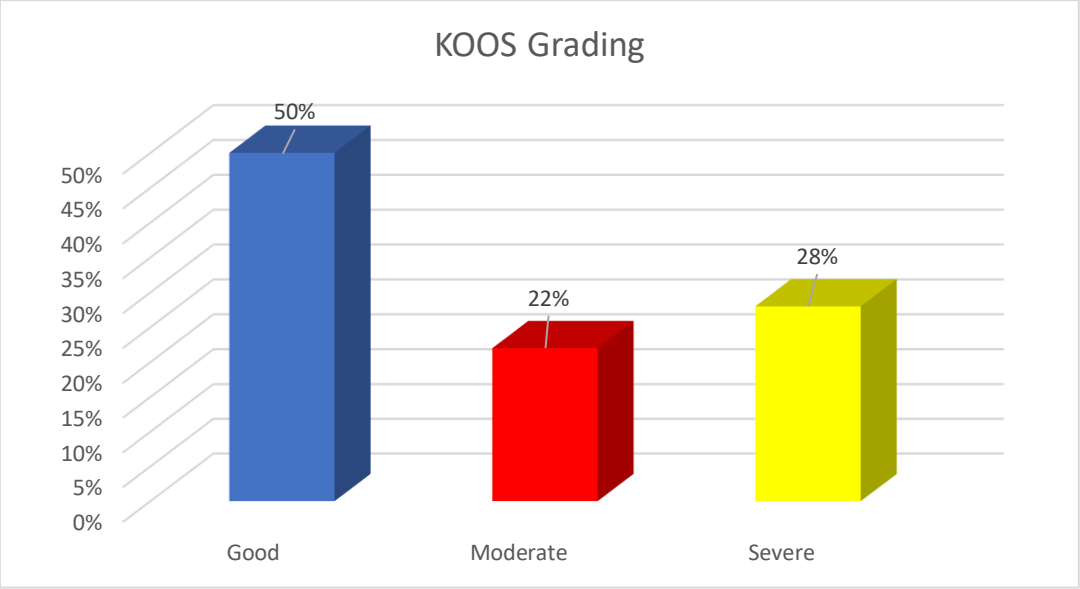

Figure 2: KOOS Grading of study participants:

Table 1: Investigation of OA patients(n=50):

Investigation	OA Grade	N	Mean	SD	P Value
Leptin	1	9	47.14333	21.308051	0.952
	2	16	51.36206	18.434369	
	3	14	50.42364	32.533980	
	4	11	53.93927	30.854076	
Adiponectin	1	9	8.04622	6.403714	0.385
	2	16	14.54394	19.326278	
	3	14	9.39864	6.470185	
	4	11	17.68882	18.717043	
Resistin	1	9	12.222	2.8173	0.128
	2	16	13.962	3.8635	
	3	14	12.564	3.2740	
	4	11	11.009	1.6040	
Calprotectin	1	9	5042.22	5584.697	<0.001
	2	16	3259.81	1857.246	
	3	14	930.00	390.492	
	4	11	886.00	118.438	
FBS	1	9	156.89	51.73	0.589
	2	16	185.88	118.00	
	3	14	148.54	42.49	
	4	11	156.45	47.90	
CRP	1	9	4.18	1.62	0.843
	2	16	3.95	1.86	
	3	14	4.93	4.88	
	4	11	4.42	1.94	
LDL	1	9	111.00	32.867	0.716

	2	16	105.00	27.403	
	3	14	111.00	34.365	
	4	11	97.64	32.758	
HDL	1	9	43.78	5.954	0.565
	2	16	42.13	5.500	
	3	14	41.14	7.675	
	4	11	39.64	7.487	

Table 2: Investigation Based KOOS Grade (n=100):

Investigation	KOOS Grade	N	Mean	SD	P Value
Leptin	Good	75	43.80	28.67	0.421
	Moderate	11	48.27	31.98	
	Severe	14	54.87	31.45	
Adiponectin	Good	75	9.48	11.39	0.09
	Moderate	11	8.34	5.23	
	Severe	14	16.74	17.01	
Resistin	Good	75	8.95	3.75	0.001
	Moderate	11	12.86	3.21	
	Severe	14	11.10	2.10	
Calprotectin	Good	75	1572.21	2670.70	0.473
	Moderate	11	865.36	181.91	
	Severe	14	946.21	368.29	
FBS	Good	75	134.56	66.546	0.486
	Moderate	11	151.73	44.791	
	Severe	14	152.54	45.573	
CRP	Good	75	3.70	2.69	0.208
	Moderate	11	5.42	5.35	
	Severe	14	4.15	2.00	
LDL	Good	75	58.92	38.56	< 0.001
	Moderate	11	117.36	34.11	
	Severe	14	95.50	31.12	
HDL	Good	75	41.41	7.391	0.431
	Moderate	11	42.45	7.408	
	Severe	14	38.93	7.416	

DISCUSSION:

In the present study, the mean age was 55.82 years in OA patients and 49.02 years in controls, with female predominance observed in both groups. The mean BMI was higher in OA patients compared to controls. Similar findings were reported by Safa A et al.[11], who observed comparable age distribution and female predominance among OA patients. Regarding OA severity, most patients belonged to Grade 2 and Grade 3 categories, whereas Safa A et al.[11] reported a higher proportion of Grade 1 and Grade 2 OA cases.

Serum resistin levels were significantly elevated in OA patients, supporting its role in OA pathogenesis. Similar results were reported by Lambova SN et al.[12] and Choe et al.[13], who demonstrated higher serum resistin levels in OA patients, particularly in radiographic OA. Elevated blood glucose levels in OA patients observed in the present study were consistent with findings by Chiba D et al.[14] and Mohajer B et al.[15] who reported worsening OA symptoms and muscle degeneration in patients with diabetes mellitus. LDL cholesterol levels were significantly increased in OA patients, whereas HDL showed no significant difference. Comparable findings were reported by Zhang K et al[16], while Schwager JL et al.[17] found no significant association between lipid profile and OA.

Although CRP levels were higher in OA patients, the difference was not statistically significant. Pearle AD et al.[18] demonstrated that elevated CRP levels may reflect increased synovial inflammation in OA. Serum calprotectin levels were markedly elevated in OA patients in the present study, similar to findings by Safa A et al.[11] and Gupta TP et al.[19], who reported significantly higher serum calprotectin levels in OA patients compared to healthy controls. ESR values were also significantly elevated in OA patients, indicating the presence of inflammatory activity associated with osteoarthritis.

CONCLUSION:

The present study highlights the significant role of inflammatory and metabolic markers in osteoarthritis. Elevated levels of calprotectin, resistin, blood glucose, LDL cholesterol, ESR, and CRP among OA patients suggest the contribution of systemic inflammation and metabolic dysfunction in disease progression. Poorer KOOS scores among OA patients further

reflect impaired knee function and reduced quality of life. These findings support the potential utility of serum calprotectin and resistin as promising biomarkers for assessing disease activity and severity in osteoarthritis.

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